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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,415	01/26/2005	Vivian I Teichberg	29147	5568

7590 06/13/2006

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EXAMINER	
GOUGH, TIFFANY MAUREEN	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/522,415	TEICHBERG, VIVIAN I	
	Examiner	Art Unit	
	Tiffany M. Gough	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-119* is/are pending in the application.

4a) Of the above claim(s) *5-9 and 29-119* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,10-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/28/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of claims 1-28, and their species, transaminase, glutamate oxalocacetate transaminase, oxaloacetate, pyridoxal phosphate, and gamma-Acetylenic GABA, in the reply filed on 05/02/2006 is acknowledged.

Claims 29-119 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claims 1-28 will be considered on the merits, in so far as they read on the elected species.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing glutamate levels by administering agents such as glutamate modifying enzymes and their co-factors, capable of reducing blood glutamate levels does not reasonably provide enablement for administering an inhibitor of a glutamate synthesizing enzyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

practice the invention commensurate in scope with these claims. Specifically, the claims recite reducing extracellular brain glutamate levels by administering an effective amount of an agent, an inhibitor of a glutamate synthesizing enzyme, capable of reducing blood glutamate levels. The claims therefore encompass using any inhibitor of any glutamate synthesizing enzymes which possess very high specificity toward their substrates. However, the sole examples provided in the disclosure use only enzymes and their substrates/co-factors. Thus, with the exception of the above stated enzymes and co-factors, and in view of the lack of any specific guidance with respect to the inhibitors, one skilled in the art would expect a trial and error process to determine whether the claimed inhibitor encompassed by the claims would apply to the disclosed application, and would further have to determine through undue experimentation, without guidance from the specification, how reduce brain glutamate levels using such inhibitors.

Further, Rumigny et al (Biochemical Pharmacology, vol.30, 1981) disclose that GABA-transaminase inhibitors and increased levels of GABA in the cerebral content usually correlate with depression of brain excitability (glutamate induced) and anticonvulsant action (see intro). Gamma-acetylenic GABA is a GABA transaminase inhibitor and has been shown to increase brain GABA levels in rats and mice. This increase exhibits and anticonvulsant effect observed in many seizures, epilepsy and convulsions (see p. 305). Gamma-acetylenic GABA because of it's action mechanism, via a Schiff base with pyridoxal phosphate, other pyridoxal phosphate dependent enzymes, such as GOT, are expected to be inhibited in a similar matter. However, after chronic administration of gamma-acetylenic GABA in rats, **increased** levels of

glutamate, seizures along with intermittent excitations and convulsions were observed (see abstract and p. 308-309). Rumigny further discloses that although GABA levels were increased, GOT activities were reduced and they suspect that the elevated glutamate levels are related to the inhibition of GOT (see p. 309, 5th paragraph). Given the observation of increased levels of glutamate in rats when injected with gamma-acetylenic GABA, one would not expect to see a decrease in glutamate levels by administering an inhibitor, such as gamma-acetylenic GABA .

Undue experimentation would be required to practice the invention as claimed due to the quantity of experimentation necessary to determine what the "effective amount" of the agent used to reduce blood levels would be, the limited amount of guidance and limited number of working examples in the specification using such inhibitor and effective amount required to achieve the claimed effect; nature of the invention; state of the prior art which teaches away from applicant's invention, i.e.administering gamma-acetylenic GABA actually increases glutamate levels ; predictability or unpredictability in the art because applicant does not provide a starting point with regards to the "effective amount" capable of reducing glutamate levels whereas the art teaches the opposite effect seen when administering the inhibitor, however the "effective amount" may produce the effect as claimed by applicant; and breadth of the claims. *In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3,4,12-14,16,17-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant claims an enzyme selected incapable of converting modified glutamate into glutamate. This in itself is confusing for the reason that one would not need an enzyme to convert glutamate to glutamate and further lacks antecedent basis because claim 1 does not claim a modified glutamate.

Further, the term "being selected incapable of..." is confusing in that it is unclear on what basis the agent is "being selected incapable of..." Does the agent not have the activity to convert or does it possess a specific property making it incapable of converting? The basis from which it is "being selected..." is not clear.

The claims, as presented, are unclear and confusing with regards to applicant's invention and therefore cannot be interpreted clearly enough to be included in the search for the instant application.

In regards to claims 3,4,12,13 and 16 it is unclear if a glutamate modifying enzyme and a modifying glutamate converting enzyme are considered the same in the instant application. Applicant uses the two terms to define the transaminase of choice, GOT in the above claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2,10,11 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/21565.

Applicant claims a method of reducing extracellular brain glutamate levels by administering, to a subject in need of, an effective amount not exceeding 1g/kg body weight, of an agent, a glutamate modifying enzyme and /or modification thereof and/or a co-factor of the enzyme.

WO 99/21565 discloses a method of treating individuals with disorders related to impaired mitochondrial and cerebral function. Such disorders include Huntington's disease which is a neurodegenerative disorder contributed by glutamate-induced neuronal death.

WO '565 discloses treating such disorders by administering a nutritional supplement/pharmaceutical composition in amounts of up to 15 g, containing a Kreb's cycle intermediate, such as oxaloacetic acid (oxaloacetate, a glutamate modifying enzyme) which is used to treat an individual with disorders related to impaired

mitochondrial and cerebral function. Such disorders include Huntington's disease which is a neurodegenerative disorder contributed by glutamate-induced neuronal death.

Although the reference does not identify that the oxaloacetic acid is capable of reducing blood glutamate levels, such a capability is intrinsic to the oxaloacetic acid. Thus, by practicing the method of WO '565 one would inherently be practicing the method as claimed.

Therefore, the reference anticipates the claimed subject matter.

Claims 1,14,15 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Geng et al (J. of Neurochemistry, vol. 68, no.6, 1997)

Applicant claims a method of reducing extracellular brain glutamate levels by administering, to a subject in need of, an effective amount not exceeding 1g/kg ,of an agent capable of reducing blood glutamate levels. Applicant claims the agent to be a co-factor, pyridoxal phosphate, of a modified glutamate converting enzyme.

Geng teaches the administration of pyridoxal phosphate to epileptic patients. The increased glutamate levels, associated with elevated etracellular load of glutamate (see abstract), were normalized, thus reduced, by the administration of vitamin B6, i.e. pyridoxal phosphate (see p.2503, second paragraph) in amounts not exceeding 1g/kg (seep.2502).

Thus, the reference anticipates the claimed subject matter.

Conclusion

Claims 1,2,4,10-15,17-25,27 and 28 are rejected . Claims 5-9 were not considered on the merits as they do not read on the elected species.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tiffany M. Gough whose telephone number is 571-272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tmg

RUTH A. DAVIS
PATENT EXAMINER